The operative time it takes to reconstruct the pericardium is not significant, and the diaphragmatic reconstruction is not facilitated in our experience by leaving the pericardium in.

Finally, we agree that personal experience with chylothorax should guide each surgeon as to whether prophylactic thoracic duct ligation should be used routinely.

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Technique for microsphere injection

To the Editor:

We read with great interest the article by Hedayati and associates[1] recently published in the *Journal*. The authors suggested that axillary artery cannulation for cardiopulmonary bypass is cerebroprotective from aortic atheroemboli by using canine models. We respectfully would like to note some procedural inconsistencies that might have lead to bias in the authors' conclusions.

The authors assessed the distribution of microspheres simulating aortic atheroemboli shed by patients during cardiopulmonary bypass. However, the microsphere injection method was inconsistent (eg, the pump flow was not constant, and the rate of microsphere injection was unclear), and the reference blood withdrawal rate for calculating tissue blood flow was unclear. Because the distribution pattern of the microspheres can be influenced easily by the pump flow rate, microsphere injection rate, shape of the aorta, and location of the injection, more precise experimental protocols might affect this study's results.

One more point of concern in this study is the size of the microspheres. Small microspheres (15 μm in diameter) have been used for measuring tissue blood flow,[2] and large microspheres (>50 μm in diameter) have been used for creating microemboli[3] by several investigators. Hedayati and associates[1] used microspheres 15 μm in diameter; however, they did not use the microspheres to measure tissue blood flow but rather as microemboli in this study. Because atheroemboli are generally larger than 15 μm in diameter and because size affects the degree of cerebral ischemia and infarction,[4] we believe that the larger microsphere should have been used to analyze the risk of atheroemboli in the aorta during cardiopulmonary bypass.

In light of these considerations, the authors' conclusion that "axillary artery cannulation for cardiopulmonary bypass is cerebroprotective" cannot be fully supported on the basis of the data presented. More studies with larger microspheres or flow characterization with both particle image velocimetry and laser Doppler velocimetry could provide more meaningful results and insights on this subject to further understand this clinically important topic.

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Reply to the Editor:

Thank you for your interest in our publication entitled "Axillary artery cannulation for cardiopulmonary bypass reduces cerebral microemboli." We are confident that our conclusion, that axillary cannulation reduces cerebral microemboli, is supported by our experimental evidence. We apologize for any lack of clarity with our experimental design. We agree that the distribution pattern of the microspheres might be influenced by the pump flow rate, microsphere injection rate, shape of the aorta, location of the injection, and location of the cardiopulmonary bypass cannulation site. Using each animal as its own control enabled us to provide constant conditions for each variable, with the only difference being the cannulation site.

Our microsphere injection method was consistent for each animal. The only variable was the cannulation site for cardiopulmonary bypass. The pump flow rate was constant during the 2 cannulation techniques within each animal, although the pump rate did vary from 1.9 to 3.4 $L \cdot min^{-1} \cdot m^{-2}$ among animals to maintain constant pressure among animals. Five million microspheres (2.5×10^6 microspheres/mL) were injected over 1 minute.

Larger microspheres have been used to induce infarction or ischemia and might have been preferred if that was our intention. We were exclusively interested in the distribution of the spheres and found no evidence that the distribution of 50-μm spheres would have, in our model, altered our impressive results. Atheroemboli range in size, with the most numerous being the smallest.[1] We used 15-μm spheres, as has been done before in similar investigations.[2]

We agree with your suggestion that further characterization of the flow pattern through particle-imaging techniques will provide additional evidence as to the superior ability of axillary cannulation to provide cerebroprotection, and we plan to do so in the future to further corroborate the vastly reduced stroke rate we have observed when axillary perfusion was used in our patients with high-risk aortas.

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Carbodissection of the internal thoracic artery

To the Editor:

I write with reference to the article by Özkan and associates titled "A Carbon Dioxide Insufflation Technique for Prepara-

tion of the Internal Thoracic Artery," which appeared in the April 2003 issue of the *Journal.*[1] This report resurrects a technique I described years ago in an article titled "Carbodissection of the Internal Thoracic Artery Pedicle," which appeared in *The Annals of Thoracic Surgery*.[2] 1 was pleased that Dr Özkan used this technique with the same success I have observed since 1988 but was disappointed that, perhaps through an oversight, Dr Özkan chose not to reference my work. The important issue is not who performed the procedure first but that Dr Özkan's observation validates the efficacy of the technique.

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doi:10.1016/j.jtcvs.2004.04.048

Reply to the Editor:

We thank Dr Lee for responding to our article and for his comments.

Carbon dioxide insufflation, as a method of preparation of the internal thoracic artery, is not novel. Dr Lee first introduced this technique in 1988.[1] Later, Bognolo and associates[2] used the same technique in 1995. We also have used the carbon dioxide insufflation technique since 2002 without citing Drs Lee and Bognolo.[3] After this omission was noticed, we referred to Drs Lee and Bognolo in our next article,[4] titled "Effect of Carbon Dioxide Insufflation on Free Internal Thoracic Artery Flows: Is it a Vasodilator?" which was published in the *Journal.* We congratulate Dr Lee for introducing this techique to heart surgery.

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doi:10.1016/j.jtcvs.2004.04.049

Early ischemic preconditioning provides transient protection

To the Editor:

We read with great interest the study by Toumpoulis and colleagues,[1] "Superiority of Early Relative to Late Ischemic Preconditioning in Spinal Cord Protection After Descending Thoracic Aortic Occlusion" published in the November 2004 issue of the *Journal.* In their experimental model, they revealed the superiority of early ischemic preconditioning (IP) in reducing spinal cord injury caused by thoracic aortic occlusion. IP is a new concept against spinal cord ischemic injury. Although previous reports have demonstrated its beneficial effects, there are still controversial issues including the fundamental mechanisms by which it provides protection and the duration of reperfusion between 2 ischemic insults.

Recent experiments revealed a delayed protective effect of IP, termed the "second window of protection," which appears more than 24 hours after the initial ischemic insult. A subgroup of protein family, called "stress proteins," which are crucial for the maintenance of cell integrity under unfavorable conditions, are accepted as an important cause of the "second window" provided by IP. These stress proteins, in particular, heat shock proteins (HSPs), are able to alter the resistance of the tissues to subsequent ischemic and nonischemic insults.[2,3]

We have also examined this known strategy, but our experience differs from that of Toumpoulis and colleagues. We used a rat model of spinal cord ischemia and revealed that hyperthermic IP (HIP) before transient aortic occlusion resulted in improved neurologic and histopathologic outcomes. In the IP group, we used an early IP model with a reperfusion interval of 30 minutes between 2 ischemic insults. In the HIP group, rats were heated to 41°C and maintained at this temperature for 15 minutes. Twenty-four hours later, the described early IP model was also applied to this group of rats. The spinal cord was extracted, and the lumbosacral region was examined under light microscopy to assess necrosis and under electron microscopy to determine HSP-ubiquitin positivity.

The neurologic evaluation of rats performed on the first day did not reveal a statistically significant difference between the IP and HIP groups. However, on the second day, we noticed a delayed neurologic deterioration in the early IP group. The neurologic scores of the HIP group were significantly higher than those of the IP group at the end of 48 hours ($P < .05$). Histologic evaluation correlated well with the neurologic outcome with lesser cellular damage in the HIP group. Ubiquitin positivity was present only in hyperthermia-pretreated animals.

On the basis of our experience, we believe that a model with a short reperfusion interval does not provide the delayed anti-ischemic effect of IP, termed the "second window," which is possibly related to the expression HSPs. Our results suggest that HSP-ubiquitin induction by heat stress may be responsible for the delayed spinal cord protection seen in this model. Whole-body hyperthermia may have important clinical implications, and further studies will delineate the fundamental mechanisms of hyperthermia-induced neuroprotection.

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